Microbiology and injury characteristics in severe open tibia fractures from combat

Travis C. Burns, MD, Daniel J. Stinner, MD, Andrew W. Mack, MD, Benjamin K. Potter, MD, Rob Beer, MD, Tobin T. Eckel, MD, Daniel R. Possley, DO, Michael J. Beltran, MD, Roman A. Hayda, MD, Romney C. Andersen, MD, John J. Keeling, MD, Harold M. Frisch, MD, Clinton K. Murray, MD, Joseph C. Wenke, PhD, James R. Ficke, MD, Joseph R. Hsu, MD, *and the* **Skeletal Trauma Research Consortium,** *Fort Sam Houston, Texas*

BACKGROUND: Type III open tibia fractures are common combat injuries. The purpose of the study was to evaluate the effect of injury characteristics and surveillance cultures on outcomes in combat-related severe open tibia fractures.

METHODS: We conducted a retrospective study of all combat-related open Gustilo and Anderson (G/A) type III diaphyseal tibia fractures treated at our centers between March 2003 and September 2007.

RESULTS: One hundred ninety-two Operation Iraqi Freedom/Operation Enduring Freedom military personnel with 213 type III open tibial shaft fractures were identified. Fifty-seven extremities (27%) developed a deep infection and 47 extremities (22%) ultimately underwent amputation at an average follow-up of 24 months. Orthopedic Trauma Association type C fractures took significantly longer to achieve osseous union ($p = 0.02$). G/A type III B and III C fractures were more likely to undergo an amputation and took longer to achieve fracture union. Deep infection and osteomyelitis were significantly associated with amputation, revision operation, and prolonged time to union. Surveillance cultures were positive in 64% of extremities and 93% of these cultures isolated gram-negative species. In contrast, infecting organisms were predominantly gram-positive.

CONCLUSIONS: Type III open tibia fractures from combat unite in 80.3% of cases at an average of 9.2 months. We recorded a 27% deep infection rate and a 22% amputation rate. The G/A type is associated with development of deep infection, need for amputation, and time to union. Positive surveillance cultures are associated with development of deep infection, osteomyelitis, and ultimate need for amputation. Surveillance cultures were not predictive of the infecting organism if a deep infection subsequently develops. (*J Trauma.* 2012;72: 1062–1067. Copyright © 2012 by Lippincott Williams & Wilkins)

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KEY WORDS: Open tibia fracture; combat injuries; blast injuries.

Severe open tibia fractures in combat are often because of multiple penetrating fragments secondary to explosive mechanisms.[1] This injury mechanism is distinct from blunt trauma that predominates in civilian trauma series.[2] In addition to these mechanisms resulting in different fracture and soft tissue wound characteristics, the contamination rate may be different secondary to the penetrating fragments, debris, and the environment in which the injuries are sustained.[3] In the current conflicts in Iraq and Afghanistan, injured service members are evacuated through three to four medical facilities before arriving at a definitive treatment facility, often a week or longer after injury.[4] Terrorist attacks on civilian targets over the past decade have increased the possibility that nonmilitary orthopedic surgeons will treat patients injured by high-energy blast mechanisms. From the attacks on the World Trade Center towers to the London subway bombing, successful attacks on civilian targets have employed surgeons to treat injuries not typically associated with civilian practice.

Open tibia fractures are the most common long bone fractures treated by orthopedic surgeons in a combat theater of operations.[5,6] Fifty-four percent of all combat-injured personnel have extremity involvement, and 82% of all long bone fractures evacuated from theater are open.[5,6] The largest previous study on combat-related tibia fractures was published after the Vietnam War on 228 open tibia fractures, but

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From the Department of Orthopedics and Rehabilitation (T.C.B., D.J.S., D.R.P., M.J.B., J.R.F., J.R.H.), San Antonio Military Medical Center, Fort Sam Houston, Texas; Department of Orthopedics and Rehabilitation (A.W.M., B.K.P., R.B., T.T.E., R.C.A., J.J.K.), Walter Reed National Military Medical Center, Bethesda, Maryland, and Washington, DC; Department of Orthopedics (R.A.H.), Brown University Warren Alpert School of Medicine, Providence, Rhode Island; Department of Medicine (C.K.M.), San Antonio Military Medical Center, Fort Sam Houston, Texas; and US Army Institute of Surgical Research (J.C.W., J.R.H.), Fort Sam Houston, Texas.

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Address for reprints: Travis C. Burns, MD, Department of Orthopedics and Rehabilitation, San Antonio Military Medical Center, 3551 Roger Brooke Dr., Fort Sam Houston, TX 78234; email: travis.burns@amedd.army.mil.

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included all open tibia fractures regardless of severity.[7] The patients were all treated with plaster cast immobilization and healing of open wounds by secondary intention. A recent small series of combat-related tibia fractures treated only with circular external fixation reported union of all fractures at an average of 221 days.[8] Little is known, however, regarding surveillance cultures, infections, and outcomes across multiple fixation methods. The purpose of this study is to evaluate the effect of injury mechanism, fracture and soft tissue classifications, and surveillance culture results on outcomes in severe open tibia fractures sustained in Operation Iraqi Freedom (OIF) and Operation Enduring Freedom (OEF).

MATERIALS AND METHODS

After protocol approval by our institutional review boards, we performed a retrospective study of all combat-related open Gustilo and Anderson (G/A) type III diaphyseal tibia fractures treated at our centers between March 2003 and September 2007. We identified 192 patients with 213 severe open tibia fractures sustained during combat operations in OIF or OEF. The service members were followed until final treatment at a military facility with average follow-up of 24.3 months (median, 21; range, 5–54). Data were collected at each participating institution from local trauma databases, operative logs, the Joint Theater Trauma Registry, electronic radiographs, and local inpatient and outpatient records. We collected injury information, Injury Severity Score, Abbreviated Injury Scale, complications, and time to radiographic union.

We defined diaphyseal as those fractures that did not extend to within 5 cm of the tibial plateau or tibial plafond.[2] The soft tissue injury was characterized based on the G/A classification.[9–11] G/A type III A fractures were associated with high-energy mechanism identified by fracture comminution, segmental fracture pattern, or soft tissue injury with traumatic laceration greater than 10 cm. Type III B fractures required a soft tissue coverage procedure, free or rotational flap, or acute shortening for wound management. Type III C fractures were associated with a vascular injury requiring repair. The fracture severity was classified according to the Orthopedic Trauma Association (OTA) AO fracture classification.[12] Neurologic injury was defined as motor or sensory dysfunction involving the peroneal or tibial nerve distal to the popliteal fossa. Surveillance cultures were obtained during the initial debridement procedure within 72 hours of arrival based on surgeon preference. Cultures defined as infection cultures were taken greater than 14 days after injury and obtained in the operating room due to concern for infection. Because patients received an average of six debridement procedures before attempted definitive wound closure, this 2-week time period ensured we were outside the window of initial debridement. Deep infections were defined as wound infections that required an unplanned return to the operating room for irrigation and debridement after wound closure or application of a negative pressure dressing. Osteomyelitis was defined as a deep infection with positive intraoperative bone cultures, radiographic changes consistent with osteomyelits, or clinical documentation of operative findings consistent with osteomyelitis. Time to radiographic union was defined as bridging callus across three of four cortices on orthogonal radiographs evaluated by one investigator at each site.[13] Reoperation was defined as an operation to revise or augment fracture fixation after arriving to a Level V facility.

Statistical Methods

Multivariate analyses were performed to assess the relationship between injury characteristics and the occurrence of adverse outcomes. Deep infection, osteomyelitis, need for amputation, need for unplanned reoperation, and time to osseous union were our primary outcome measures. We evaluated these on the basis of injury mechanism, fracture severity, G/A classification, presence of segmental bone loss, surveillance cultures, and surveillance organism (gram-negative or positive, multiple or single bacterial growth, and for specific bacteria). The collected data were then analyzed for statistical significance of observed differences in outcomes.

Descriptive statistical analysis for demographic data included the means/standard deviations or medians/range as appropriate. Continuous variables and scores were compared via the Wilcoxon test for nonparametric and score data and Student's t test for parametric data. Dichotomous variables were compared using the χ^2 test or Fisher's exact test as appropriate. All reported p values are two tailed with an $\alpha \leq 0.05$ determining statistical significance. Statistical analysis was performed with SAS 9.1 (Cary, NC).

RESULTS

Grade III Tibia Fractures Sustained in OIF/OEF: Mechanism and Classification

The typical service member in this cohort was a young, male injured by an explosion (Table 1). Approximately, half of the type III open tibia fractures were G/A type III A, and the majority of the fractures were classified as an OTA type C. The patients had average Injury Severity Score and Abbreviated Injury Scale scores of 14.62 and 3.45, respectively. Neurologic injury occurred in 22% of the fractures, and 11.7% of the injuries were associated with a vascular injury requiring repair.

Early Outcomes and Complications

The average time to union was 9.2 months (median, 7.7; range, 3–49; Table 2). Time to union was not significantly associated with mechanism of injury ($p = 0.18$) or presence of segmental bone loss ($p = 0.34$). Presence of initial bacterial contamination approached significance for time to union ($p = 0.053$). G/A classification and OTA fracture classification were significantly associated with a prolonged time to union with increasing severity of the scoring system ($p = 0.001$, $p = 0.015$). Forty-seven extremities (22%) required an amputation for definitive management at an average of 2.5 months (median, 0.4; range, 0.2–18) after injury. Thirty-six patients required an amputation within 3 months of their injury, whereas 11 were performed in a delayed fashion.

Amputation was not significantly associated with mechanism of injury ($p = 0.39$), OTA fracture classification

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TABLE 1. Tibia Fracture Injury Characteristics and Demographics

	Number or Mean	Median or Percent
Age (yr)	25.6	24.0
Mechanism (%)		
Blast	172	80.8
GSW	20	9.4
MVA	18	8.5
Other	3	1.4
Gustilo and Anderson		
III A	112	52.6
III B	76	35.7
III C	25	11.7
OTA		
A	34	16.0
B	60	28.2
C	119	55.9
Segmental bone loss	15	7
Peripheral neurologic injury	44	22
ISS	14.62	10
AIS score	3.45	3

MVA, motor vehicle accident; GSW, gunshot wound; ISS, Injury Severity Score; AIS, Abbreviated Injury Scale.

TABLE 2. Type III Open Fracture Outcomes and Complications

	Number or Time	Median or Percent
Time to follow-up (mo)	24.3	21
Time to radiographic union (mo)	9.2	7.7
Revision operations	1.6	1
Deep infection	58	27.2
Osteomyelitis	36	16.9

($p = 0.069$), or the presence of bone loss ($p = 0.53$). Ultimately, need for amputation was associated with G/A classification ($p = 0.0001$) with the highest amputation rate in the type III C subgroup (72%).

The service members required on average 1.6 (range, 0–11) additional surgical procedures aimed at achieving osseous union. Mechanism of injury ($p = 0.38$), G/A classification ($p = 0.15$), OTA fracture classification ($p = 0.38$), presence of segmental bone loss ($p = 0.54$), or initial bacterial contamination ($p = 0.94$) were not associated with the need for reoperation.

Subgroup Analysis: Infections

There were 57 open fractures (26.7%) that developed a deep infection requiring operative intervention. Of the 57 deep infections, 35 had culture positive bone specimens diagnostic for osteomyelitis (16.4%).

Compared with G/A type III A fractures (20.5%), type III C fractures (44%) were more likely to develop a deep infection ($p = 0.03$). There was no difference in deep infection or osteomyelitis rate based on mechanism of injury ($p = 0.42$ and $p = 0.60$).

Culture specimens were obtained in 145 extremities during the initial evaluation period at the study centers (Table 3). Of the patients who had surveillance cultures taken during the initial irrigation and debridement procedure, 64% (93) had bacterial growth (Fig. 1). Positive initial surveillance

TABLE 3. Type III Open Fracture Culture and Infection

	Number	Percentage
Surveillance cultures	**145**	
Culture positive	93	64.1
Gram-negative	85	91.4
Gram-positive	24	25.8
Polymicrobial	32	34.4
Most common isolates		
Acinetobacter baumannii	57	61.3
Enterobacter cloacae	17	18.3
Klebsiella pneumoniae	13	14
Enterococcus faecium	13	14
Pseudomonas aeruginosa	13	14
Staphylococcus epidermidis	6	6.5
Infection cultures	**57**	
Culture positive	51	89.5
Gram-negative	26	52
Gram-positive	34	68
Polymicrobial	12	23.5
Surveillance culture matching any organism in infection culture	11	26.2
Surveillance culture same as infection culture	3	7.1
Most common isolates		
Staphylococcus aureus	18	35.3
MRSA	10	
MSSA	8	
Acinetobacter baumannii	10	19.6
Staphylococcus epidermidis	10	19.6
Klebsiella pneumoniae	6	11.8
Enterococcus faecium	4	7.8

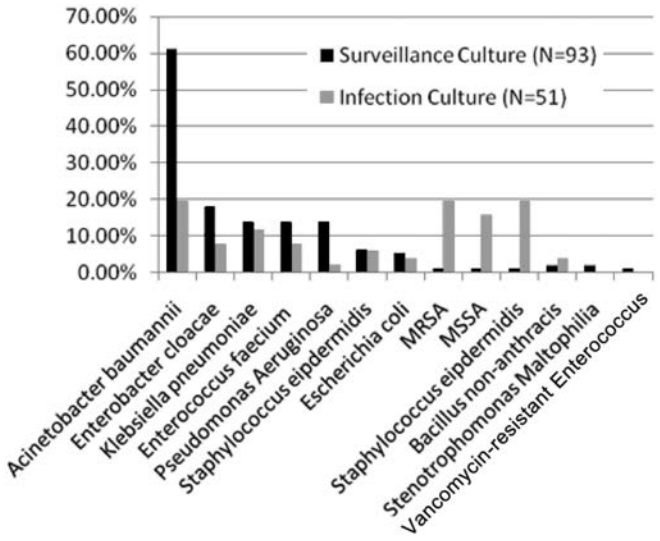

Figure 1. Incidence of bacteria in surveillance and infection cultures.

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cultures were associated with subsequent development of deep infection ($p = 0.0005$), osteomyelits ($p = 0.0012$), and need for amputation ($p = 0.01$). In addition, the more bacteria identified on surveillance cultures, the more likely the patient was to develop a deep infection ($p = 0.005$) and osteomyelitis ($p = 0.0017$). Compared with negative surveillance cultures, the odds ratio of developing a deep infection if one bacteria is cultured is 2.85 (95% confidence interval, 1.42–5.75) while this increases to 3.22 (95% confidence interval, 1.38–7.53) if two or more bacteria are cultured. There was no significant association between specific bacteria or gram staining and subsequent development of a deep infection, amputation rate, or time to union.

Of the initial culture positive wounds, 38.7% (36 of 93) ultimately developed a deep infection compared with 11.5% (6 of 52) of initially culture negative wounds ($p = 0.0005$). Of those patients who developed a deep wound infection and had initial cultures obtained, 11 of the 42 (26.2%) cultures matched at least one of the initial surveillance organisms. Eight of these 11 with the same initial culture and infection culture were polymicrobial and only matched one organism. In all three cases with the same surveillance and deep infection culture organisms, *Acinetobacter baumannii* was the sole organism identified in early deep wound infections. Specific identification of the ultimate infecting pathogen occurred in only 7% of the positive surveillance cultures and only 2% of all surveillance cultures taken.

In contrast to the largely gram-negative initial culture results, the 57 deep wound infections were predominately gram-positive phenotypes. Bacterial cultures were positive for 51 of the 57 deep infections, whereas the remaining 6 deep infections were clinically considered culture-negative deep infections. Methicillin-resistant *Staphylococcus aureus* (MRSA) was the most commonly isolated organism in deep infections.[10] Two were identified in patients who did not have a surveillance culture, and six of the remaining eight MRSA infections were isolated in patients who had a different positive surveillance culture.

Patients who had a deep infection or osteomyelitis had a higher rate of amputation (40.4% and 34.3%) than those extremities not complicated by infection (15.4%, $p = 0.0002$, $p = 0.02$; Table 4). Patients with a deep infection or osteomyelitis, also, had a significantly longer time to union (11.2 and 11.0 months) and higher reoperation rates (2.37 and 1.97) compared with those extremities not complicated by infection (8.6 months, $p = 0.0002$ and $p = 0.001$).

TABLE 4. Infection Effect on Amputation and Osseous Union

	Amputation Rate (%)	*p*	Time to Union (mo)	*p*
No infection (156)	15.5		8.64	
Deep infection (57)	40.4	0.0002*	11.15	0.0002*
Osteomyelitis (35)	34.3	0.02*	11.02	0.001*

* *p* values compare deep infection and osteomyelitis to no infection.

DISCUSSION

In the largest known series of combat-related type III open tibia fractures, we recorded an 80.3% union rate at an average of 9 months after injury. There were 47 fractures that required an amputation (22%) and 57 open fractures that developed a deep infection (27.2%). Positive surveillance cultures were associated with an increased risk of deep infection, osteomyelitis, and ultimate need for an amputation. Deep infection and osteomyelitis were further associated with prolonged times to fracture union and a higher reoperation rate. The cultures, however, were not useful for predicting the infecting pathogen if an infection did occur. Specific identification of the ultimate infecting pathogen occurred in only 7% of the positive surveillance cultures and only 2% of all surveillance cultures taken.

Patients with a deep infection or osteomyelitis had a significantly longer time to union (11.2 and 11.0 months), higher amputation rates (40.4 and 34.3%), and required more revision operations (2.37 and 1.97) compared with those extremities not complicated by infection (8.7 months, $p = 0.0002$; 15.4%, $p = 0.0002$; 1.45, $p = 0.0001$). Mechanism of injury was not predictive of outcomes, while OTA fracture classification was only predictive of a longer time to union in type C fractures. More severe soft tissue injury according to G/A classification was associated with increased rates of deep infection, need for amputation, and prolonged time to union.

Severe open tibia fractures are common injuries treated at civilian trauma centers. The mechanisms of injury are predominately motor vehicle collisions, falls from height, and pedestrians struck by motor vehicles.[2,14–18] In contrast to these commonly reported mechanisms, open tibia fractures sustained in the current combat environment are most commonly because of multiple or single penetrating trauma from blast mechanisms and gunshot wounds. The resulting soft tissue trauma and contamination associated with "outside-in" mechanisms may be different from the corresponding civilian injuries. The differences in injury mechanism and severity may therefore portend a different prognosis than civilian injuries.[8,19,20]

The distribution of open tibia fractures in our series according to the G/A system had a relatively larger percentage of type III A (52%) injuries compared with civilian series, which may be because of a difference in subgroup inclusion criteria.[2,21] According to the OTA fracture classification, 55% of the injuries in our series were in the most severely comminuted, type C category, a substantially higher proportion than reported in published civilian series (e.g., 18% in Court-Brown and McBirnie).[2]

Infection rates after open fractures sustained during combat range from 1% to >50% and may be influenced by injury inclusion criteria and infection definitions.[11,22,23] Previous reports of war-related wound infections identified gram-negative bacteria as the predominant phenotype.[24,25] A report of infectious complications after open tibia fractures from the current conflicts in Iraq and Afghanistan revealed predominately gram-negative organisms early in the clinical course, whereas all recurrent infections were gram-positive infections.[26] A series of 85 combat-related mangled extrem-

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ities in British military casualties revealed a 24% infection rate and a 6% rate of osteomyelitis.[25] In an analysis of their culture results, *Acinetobacter* was recovered at a median of 6 days after injury and *S. aureus* was recovered at a median of 36 days after injury. The predominance of *A. baumannii* in our initial cultures was similar to previous reports of gram-negative organisms from the conflicts in Iraq and Afghanistan.[26,27] Our trends in this series thus follow-up earlier smaller series noting gram-negative organisms most commonly on surveillance cultures within 72 hours of arrival and a predominance of gram-positive infections as the infecting pathogens later in the clinical course.

Positive initial surveillance cultures in our series correlated with subsequent development of deep infection, and this is consistent with previous reports in the civilian literature.[28] Also consistent with the civilian data, these initial surveillance cultures did not accurately predict subsequent infecting pathogens for deep infection or osteomyelitis.[28,29] The data may be interpreted in a number of ways. First, antibiotic treatment of the positive surveillance cultures may have selected for organisms resistant to those antimicrobial agents or, at least, different organisms. Supporting this interpretation, six of the eight (75%) MRSA infections in patients with surveillance cultures came from patients with a positive surveillance results. On the other hand, initial positive surveillance cultures, and the clinical decision to obtain such cultures, may be an indicator of soft tissue injury severity. The more severe soft tissue injury has greater contamination, longer time to wound closure and definitive stabilization, and higher rates of subsequent complications. This interpretation is supported by the higher amputation rate and a trend toward prolonged time to union ($p = 0.053$) observed in patients with positive surveillance cultures.

Initial antimicrobial therapy in the combat zone may have masked recovery of pathogens in surveillance cultures but did not eradicate deep-seated infection and allowed only the gram-negative pathogens to be seen on initial screening cultures in the United States. Finally, nosocomial transmission may have occurred as the patients had multiple surgeries, prolonged stays in the hospital, and frequent interactions with the healthcare environment. Because positive surveillance cultures were associated with subsequent development of infection, number of procedures, and development of deep infection, surveillance cultures theoretically could be used to alter antibiotic prophylaxis or debridement procedures. Further characterization of injury care from point of injury through the evacuation chain with genotypic comparison of infecting and colonizing bacteria over time and antimicrobial therapy are needed to answer these theories.

This study is retrospective in nature and retains the associated weaknesses, potential biases, and limitations inherent to retrospective studies. Fracture and wound management, although similar, were not standardized between patients, surgeons, or institutions. Failure to observe differences between groups may be because of inadequate power in the study. Initial surveillance cultures were not performed in an uniform manner and may have a selection bias for the most severe wounds. Initial surveillance cultures were only available after arrival at our facilities, and no in-theater antimicrobial therapy information was available because of limitations associated with accessing data from care provided in a combat region and overseas.[26] The intra- and interobserver reliability of the classification schemes used is low, although they are commonly used within the orthopedic trauma community.[30,31] These classification schemes, however, were not the basis for the majority of our comparisons and thus their reproducibility should not substantively affect the study results.

Patients who return from a combat theater with a type III open tibia fracture have a 27% risk of deep infection and a 22% rate of amputation. The degree of soft tissue injury and development of deep infection were important factors in determining patient outcomes. Surveillance cultures were predictive of development of deep infection, osteomyelitis, and need for amputation but not for the ultimate infecting organism. Patients with a deep infection or osteomyelitis, also, had a significantly longer time to union and higher reoperation rates. The utility of surveillance cultures to guide early antibiotic management, additional wound debridement, and method of fracture fixation must be delineated with future research.

AUTHORSHIP

T.C.P., A.J.S., R.A.H., R.C.A., J.J.K., H.M.F., L.K.M., J.R.F., and J.R.H. conceived of this study, which was designed by T.C.P., A.J.S., B.K.P., R.A.H., R.C.A., J.J.K., H.M.F., L.K.M., and J.R.H. Data acquisition was performed by T.C.P., A.J.S., A.W.M., R.B., T.T.E., D.R.P., and M.J.B. J.R.H. analyzed these data. T.C.B., A.J.S., and J.R.H. drafted the manuscript. All authors participated in critical revision and approval of the final manuscript.

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DISCLOSURE

The authors declare no conflicts of interest.

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